

Notice of Allowability**Application No.**

09/600,661

Applicant(s)

LINSCHOTEN ET AL.

Examiner

Thomas McKenzie, Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to amendments of 9/15/04.
2. ☒ The allowed claim(s) is/are 1-9, 12, 14-25 and 29.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

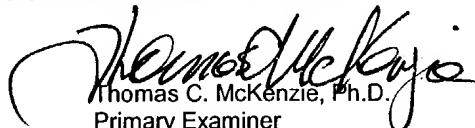
* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 151113 & 9/15/04
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____


Thomas C. McKenzie, Ph.D.
Primary Examiner
Art Unit 1624

Inventorship

1. In view of the papers filed 9/22/04, the inventorship in this nonprovisional application has been changed by the deletion of Peder Svensson. The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

EXAMINER'S AMENDMENT

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee. Authorization for this examiner's amendment was given in a telephone interview with Richard Sterner on 12/10/04. The application has been amended as follows: please enter the amendments to claims 12, 16, and 17 as shown below. Please add new claim 29.

12. (currently amended) A method for inhibiting carboxypeptidase U, comprising administering an effective amount of a compound according to any one of claims 1-5.

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16. (currently amended) A method both for inhibiting carboxypeptidase U and for achieving an antithrombotic effect via a different mechanism, which method comprises administering a therapeutically effective total amount of:

- (i) a compound of Formula I according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier; and
- (ii) one or more antithrombotic agents selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P_2T) antagonist, in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

17. (currently amended) A method both for inhibiting carboxypeptidase U and for achieving an antithrombotic effect via a different mechanism, which method comprises administering the formulation according to claim 14.

29. (new) A method for treatment of thrombosis and hypercoagulability, comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1-5.

Statement of Reasons for Allowance

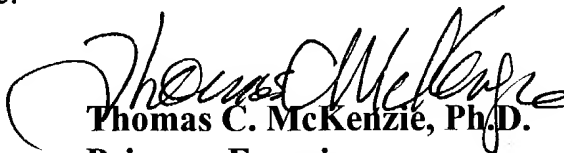
3. Claims 1-9, 12, 14-25, and 29 are allowed. The following is an Examiner's statement of reasons for allowance: Applicants amendments to the claims and the new title overcome the two objections made in points #3 and #4 of the previous office action. The deletion of "prophylaxis" and "susceptible to" from the use claims, made in the present Examiner's amendment overcomes the enablement rejection made in point #5. The evidence supplied by Applicants, namely the scientific papers Barrow (J. Med. Chem.), Muto (Eur. J. Pharmacol.), Suzuki (J. Pharmacol. Exper. Ther.), Hashimoto (Thromb. Haest.), Wu ((Thromb. Haest.), Nagashima (Thromb. Res.), and Redlitz (Circulation) prove that carboxypeptidase U inhibitors, like those of the Applicants, are efficacious in monkeys, rats, rabbits, and dogs in art-recognized disease models of thrombosis and hypercoagulability. Treatment of these two diseases has support in line 6, page 17 of the specification and is enabled. Thus, new claim 29 is allowable. The present Examiner's amendments to claims 12, 16, and 17 removes reference to treatment of "conditions associated with inhibition of carboxypeptidase U". Applicants have proffered testing data to show that 40 of their compounds inhibit the enzyme carboxypeptidase U (CPU). Thus, there can be no question as to the ability of their compounds to inhibit CPU and the enablement rejection to claims 12, 16, and 17, made in point #6, is overcome. The deletion of "conditions associated with inhibition of carboxypeptidase U" also overcomes the indefiniteness rejection made in point #7.

4. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

5. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). All Post-Allowance correspondence concerning this application must be mailed to the following address:

Box Issue Fee
Commissioner for Patents
Washington, DC 20231.

Such correspondence (amendments under 37 CFR 1.312, IDS statements, formal drawings etc) also may be faxed to the Office of Patent Publications at (703) 308-5083. Sending Post-Allowance papers to Technology Center 1600 will only cause delays in matching papers with the case.


Thomas C. McKenzie, Ph.D.
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